

REMARKS

The claims remain rejected under 35 U.S.C. § 103(a) as obvious over Carrano *et al.*, Groswasser *et al.*, Stites *et al.*, and Bouvet *et al.* For the following reasons, the applicants respectfully traverse.

This paper is formally responsive to the Office Action mailed September 22, 2005, but addresses the Advisory Action mailed June 2, 2005. The applicant stands by and reiterates the arguments set forth in their after-final response filed February 22, 2005.

The Advisory Action continued to maintain that one would expect a greater immune response closer to the site of injection. In support of this allegation, the Office Action posited the following theory of action:

The antigen injected in the thigh area is delivered to the lympho [sic] nodes initially via the femoris vein. For specific immunoglobulin induction in a lymph node, the closer to the femoris vein circulation, the faster and greater the immune response will likely be.

But this is simply incorrect. The injected antigen is not delivered to the lymph system initially via the femoris vein. Once administered to the thigh muscle, the antigen first enters the lymphatic system, which brings it to the lymph nodes. Then, at the end of the lymphatic pathway, the antigen reaches the blood circulation at the level of the upper chest via the subclavian vein (just under the clavicle).

Furthermore, as the data in the second Declaration of Therese-Marie Jourdier demonstrated and Dr. Jourdier attested, a greater immune response is observed in vaginal and rectal secretions of subjects having received antigen in the thigh compared to subjects having received antigen directly through vaginal and rectal routes. This empirical evidence contradicts the expectation posited in the Office Actions that a greater immune response would be observed closer to the site of injection. As the data demonstrated, distal injection in the thigh gave a greater immune response observed in vaginal and rectal secretions compared to most proximal administration via the vaginal and rectal routes.

The Office Action dismissed the significance of this observation, alleging that the data were without a control. But this too is not correct. The data includes a negative control corresponding

to the data obtained with an administration done directly at the site where the response is expected.

Further in regard to the control issue, the Advisory Action stated there was no “control” experiment to answer the following questions:

- 1) Whether other muscular injection site is able to induce a similar pattern of systemic and local specific immune response as compared with thigh injection,
- 2) Whether such immune response only occurs to the claimed sexual transmitted disease, in other words, if injection of other pathogen in the thigh area does not induce such pattern of specific immune response.

But the data were not presented to answer these inquiries, nor are the answers to these inquiries necessary to demonstrate the patentability of the presently claimed method. The data were presented to address the specific assertion that the ordinary artisan would expect to observe a greater immune response nearer the site of an antigen injection; the data demonstrate that for the claimed invention the immune response is lesser closer to the site of administration.

Furthermore, ascertaining whether injection to the thigh differs from injection to other muscles or whether sexually transmitted pathogens differ compared to other pathogens is not necessary for patentability purposes. Rather, patentability is demonstrated by the unexpected results presented in Dr. Jourdier’s second Declaration, *i.e.*, that a greater immune response was observed in the vaginal and rectal secretions when administration was to a distal site (the thigh) compared to local administration (vaginally and rectally). This observation is in direct contradiction to the expectation agreed upon by the Examiner and Dr. Jourdier, that one would expect to improve the immune response at the targeted mucosal sites by administration directly to that site rather than distally (to the thigh). And Dr. Jourdier further attests that she is unaware of any basis by which one of ordinary skill in the art could have expected that administration to the thigh would result in a specific targeted response in a distal area, generally, and in the rectogenitourinary lymph node system and mucous membranes, in particular. Significantly, none of the art cited by the Examiner as the basis for this obviousness rejection teaches or suggests the properties observed with the presently claimed method. On the basis of these unexpected results, the presently claimed method cannot be obvious.

Despite the foregoing, however, the applicant presents a third Declaration of Therese-Marie Jourdier in which Dr. Jourdier presents data demonstrating that administration of ALVAC vCP205 and HIV gp160 antigens to the thigh yields a substantially and significantly greater specific anti-gp160 IgA immune response in the rectogenitourinary region compared to administration to the deltoid. This demonstrates that the results observed with administration to the thigh are not shared with all other muscles/muscle groups.

Further with regard to the second point (whether similar results would be manifested with other pathogens), the issue is inapposite. The claims are directed to methods of eliciting an immune response in the rectogenitourinary mucous membranes. Results with pathogens targeting other areas (*e.g.*, respiratory pathogens targeting the lungs) are not relevant. One skilled in the art would not use a route of administration leading to rectogenitourinary protection if they were seeking to treat a pathogen targeting another site in the body.

In view of the foregoing, and for the reasons previously proffered, the applicant respectfully requests reconsideration and withdrawal of the pending § 103 rejection.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

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Respectfully submitted,



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